Complete Summary

GUIDELINE TITLE

Evidence-based clinical practice guidelines: primary monosymptomatic nocturnal enuresis in primary care.

BIBLIOGRAPHIC SOURCE(S)

Asociación Española de Pediatría de Atención Primaria (AEPap). Evidence-based clinical practice guidelines: primary monosymptomatic nocturnal enuresis in primary care. Rev Pediatr Atencion Prim 2005 Oct;VII(Suppl 3):1-149.

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 04, 2007, Desmopressin Acetate (DDAVP, DDVP, Minirin, & Stimate): New information has been added to the existing boxed warning in Desmopressin's prescribing information about potential increased risk for severe hyponatremia and seizures.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Primary monosymptomatic nocturnal enuresis

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Pediatrics
Urology

INTENDED USERS

Health Care Providers
Nurses
Physicians

GUIDELINE OBJECTIVE(S)

To provide evidence-based clinical practice guidelines that analyze the evidence and help in the decision-making process of prevention, diagnosis, and treatment of primary monosymptomatic nocturnal enuresis (PMNE)

TARGET POPULATION

Children with primary monosymptomatic nocturnal enuresis (PMNE) (i.e., children 5 years of age or older, attended in Primary Care, who have not had a dry period lasting for 6 months or longer)

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention/Risk Assessment

1. Toilet training strategies (for prevention of incontinence)
2. Risk factor assessment (comorbid conditions such as chronic headache or attention-deficit hyperactivity disorder, constipation/encopresis, sleep apnea)

Diagnosis

1. Clinical interview
2. Clinical examination

3. Bladder diary
4. Dipstick urinalysis

Treatment

1. Simple behavioral interventions
2. Complex and educational behavioral interventions
3. Alarm intervention
4. Pharmacological treatment:
    - Desmopressin (intranasal, oral)
    - Desmopressin associated with anticholinergics (not recommended routinely)
5. Follow-up and withdrawing treatment

MAJOR OUTCOMES CONSIDERED

- Response to treatment assessed in terms of:
    - Initial success (14 consecutive dry nights)
    - Complete dryness (100% dry nights)
    - Full response (>90% decrease in wet nights versus baseline)
    - Cure (initial success or full response, without relapse)
- Quality of life
- Patient and parental satisfaction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Systematic Strategy for the Bibliographic Search

The systematic review of the literature only covered studies reported in Spanish, English and French. Searches were made in:

Secondary Sources of Information

Major

1. Cochrane Collaboration
2. Clinical practice guides (CPGs):
    - Centers that prepare CPGs: American Academy of Pediatrics, New Zealand Guidelines Group, Cincinnati Children's Hospital Medical Center
    - CPG storage centers: National Guideline Clearinghouse, CMA Infobase, Primary Care Clinical Practice Guidelines, NeLH Guideline Finder

3. Reports by Health Technology Assessment Agencies: Health Technology Assessment Database-HTA

Minor

4. Journals with structured abstracts: ACP Journal Club, Clinical Evidence on line, Bandolier
5. Files of critically appraised topics: AEPap, CATs

Global

6. EBM databases: TRIP/SUMSearch and The Database of Abstracts of Reviews of Effectiveness-DARE)

Primary Sources of Information

1. Traditional bibliographic databases: Medline with its electronic version PubMed, Embase, IME
2. Traditional medical journals
3. Textbooks

Grey Literature/Manual Search

Selection Criteria (Inclusion-Exclusion)

Studies were selected according to the following criteria in the searches:

- They should deal with children and adolescents. PubMed goes up to 18 years of age (in exceptional cases, and when there was no data exclusively obtained on children and adolescents, authors accepted mixed inclusion with adults, with explicit reference made in the text).
- They should deal with primary monosymptomatic nocturnal enuresis (PMNE).
- Outpatient setting: If specific information was not available according to these criteria, studies with general criteria were included (e.g., hospital setting, different types of enuresis), but this was always specified in the results.
- Quality criteria: The highest quality articles have always been selected on each aspect evaluated.
- Years of searches: Searches were made in databases from the lower limit of each one up to August 2004.

Types of Studies Included

Studies of Associated Factors in PMNE

- Systematic reviews
- Cohort studies
- Case-control studies
- Case studies
- Population surveys

Diagnostic Studies

- Validation of diagnostic tests
- Systematic reviews
- Cohort studies
- Case-control and cross-sectional studies

Treatment Studies

- Systematic reviews and meta-analyses
- Controlled clinical trials
- Cohort and case-control studies
- Case studies

The specific key words for each subject critically assessed are described in Table IX of the original guideline document. The details of the search strategy for each subject are presented in Chapter 6 of the original guideline document.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

Level		Therapy/Prevention Aetiology/Harm	Prognosis	Diagnosis	Differential Diagnosis/Symptom Prevalence Study	Economic and Decision Analyses
I	**At Least One Controlled Clinical Trial Appropriately Randomized**					
	a	SR (with homogeneity[a]) of RCTs	SR (with homogeneity[a]) of inception cohort studies; CDR[b] validated in different populations	SR (with homogeneity[a]) of Level 1 diagnostic studies; CDR[b] with 1b studies from different clinical centres	SR (with homogeneity[a]) of prospective cohort studies	SR (with homogeneity[a] of Level 1 economic studies
	b	Individual RCT (with narrow Confidence Interval[c])	Individual inception cohort study with > 80% follow- up; CDR[b]	Validating[k] cohort study with good[i] reference standards; or CDR[b] tested	Prospective cohort study with good follow-up[m]	Analysis based on clinically sensible costs or alternatives;

Level		Therapy/Prevention Aetiology/Harm	Prognosis	Diagnosis	Differential Diagnosis/Symptom Prevalence Study	Economic and Decision Analyses
			validated in a single population	within one clinical centre		systematic review(s) of the evidence; and including multi-way sensitivity analyses
	c	All or none[d]	All or none case series	Absolute SpPins and SnNouts[g]	All or none case series	Absolute better-value or worse-value analyses[j]
II	**Cohort Studies and Studies of Final Outcomes**					
	a	SR (with homogeneity[a]) of cohort studies	SR (with homogeneity[a]) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity[a]) of Level >2 diagnostic studies	SR (with homogeneity[a]) of 2b and better studies	SR (with homogeneity[a] of Level >2 economic studies
	b	Individual cohort study (including low quality RCT; e.g., < 80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR† or validated on split-sample[f] only	Exploratory[k] cohort study with good[i] reference standards; CDR[b] after derivation, or validated only on split-sample[f] or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
	c	"Outcomes" research, ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
III	**Case-controls**					
	a	SR (with homogeneity[a]) of case-control studies		SR (with homogeneity[a]) of 3b and better studies	SR (with homogeneity[a]) of 3b and better studies	SR (with homogeneity[a] of 3b and better studies

Level		Therapy/Prevention Aetiology/Harm	Prognosis	Diagnosis	Differential Diagnosis/Symptom Prevalence Study	Economic and Decision Analyses
	b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
IV		Case-series (and poor quality cohort and case-control studies[e])	Case-series (and poor quality prognostic cohort studies[l])	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
V		Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Notes:

Users can add a minus-sign "-" to denote the level of evidence that fails to provide a conclusive answer because of:

– EITHER a single result with a wide Confidence Interval (such that, for example, an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm)

– OR a Systematic Review with troublesome (and statistically significant) heterogeneity.

– Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

[a] By homogeneity the guideline authors mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome

heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.

[b] Clinical Decision Rule. (These are algorithms or scoring systems which lead to a prognostic estimation or a diagnostic category.)

[c] See note #2 for advice on how to understand, rate and use trials or other studies with wide confidence intervals.

[d] Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

[e] By poor quality cohort study the guideline authors mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study the guideline authors mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

[f] Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.

[g] An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.

[h] Good, better, bad and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.

[i] Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.

[j] Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.

[k] Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g., using a regression analysis) to find which factors are 'significant'.

[l] By poor quality prognostic cohort study the guideline authors mean one in which sampling was biased in favour of patients who already had the target outcome, or the measurement of outcomes was accomplished in <80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.

[m] Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (e.g., 1 to 6 months acute, 1 to 5 years chronic)

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Any content whose scientific evidence was insufficient is referred to explicitly. In these cases, the recommendation was reached by consensus on the basis of standard of care in the Primary Care setting. The "Centre for Evidence-Based Medicine" (CEBM) of Oxford classification was used to grade the evidence (see "Rating Scheme for the Strength of the Evidence" above). The guideline authors considered potential clinical differences between the target population of their guidelines and studies reported in the literature; for example, when the reported study's scenario was not the community but rather the hospital or any other scenario different from Primary Care, or if the study reported on a type of enuresis different from primary monosymptomatic nocturnal enuresis (PMNE). In this case extrapolation criterion were applied to grade recommendations.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Guidelines for the appropriate decision making process of prevention, risk factors, diagnosis and treatment of primary monosymptomatic nocturnal enuresis (PMNE) are based on critical review of the available data and expert consensus.

Formulation of Clinical Questions

- The clinical questions were clearly defined and all alternatives to the decision and expected outcomes were identified.
- All existing evidence was located systematically, evaluated critically, and then classified according to evidence-based medicine criteria, summarizing the best scientific evidence on each aspect.
- Each of the decision points was identified where it was necessary to integrate this valid evidence with the clinician's expertise and patient preferences. Hence, the present guide is not of a regulatory nature, it sets out to accurately identify the range of potential decisions and to provide evidence that, together with clinical judgment, patient values and expectations, and the center's conditions, should make it easier to make the most appropriate decision in each case.

The authors identified areas of uncertainty regarding associated factors, diagnosis, and treatment of primary PMNE.

Questions Identified

The areas of uncertainty were specified in the following questions:

Risk Factors Associated with Enuresis

1. Is there any physical condition that is associated with PMNE?
2. Is there any psychiatric condition that is associated with PMNE?

Diagnosis

1. Does a urine culture or dipstick urinalysis need to be performed on all children with PMNE seeking care at the Healthcare Center?
2. Do other diagnostic tests need to be carried out in children with PMNE seeking care at the Healthcare Center?

Treatment

1. How efficacious is behavioral therapy?
2. How efficacious is alarm behavioral therapy for enuresis?
3. How efficacious is drug treatment with desmopressin?
4. Have risk factors for treatment failure been described for the different treatments?

Follow-up

1. For how long should treatment be continued?
2. What is the most effective treatment withdrawal guideline?
3. What are the indications for referral to an urologist?

Timeline of the Elaboration of the Guidelines

The working meetings took place from January 2004 to May 2005, approximately every two weeks and outside of working hours.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

A. Consistent level 1 studies
B. Consistent level 2 or 3 studies or extrapolations* from level 1 studies
C. Level 4 studies or extrapolations* from level 2 or 3 studies
D. Level 5 evidence or troublingly inconsistent or inconclusive studies of any level

*Extrapolations are when data is used in a situation which has potentially clinically important differences than the original study situation.

Phillips B, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, Dawes M. Levels of evidence and grades of recommendations, 1998. Review May 2001. Center for Evidence-Based Medicine (CEBM) of Oxford Available in English at: http://www.cebm.net.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The external review took place between January and February 2005 and the assessment of applicability to Primary Care is still pending completion.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the grades of recommendations (**A, B, C, D**) are provided at the end of the "Major Recommendations."

Prevention

The following attitudes have been shown to be beneficial in achieving daytime urinary continence at an earlier age and avoiding dysfunctional voiding. Although it is not known if they will also bring about the onset of nocturnal urinary continence, it is recommended **[C]**:

- Start toilet training before the age of 18 months, perhaps when the child is able to wake up dry from his/her nap.
- Use of a pot or potty chair that properly supports his/her thighs and feet.
- Suggest to the child that they should urinate when you see or imagine that they feel the urge, so that they can do so on the first try. Do not keep the child seated on the pot until he/she urinates and do not insist that they strain if the first attempt fails.
- Be persistent in this training, because the objective can be achieved in less than three months. Do not dilute the effort by continually changing the technique.

Risk Factors Associated with Primary Monosymptomatic Nocturnal Enuresis (PMNE)

(See Table II "Factors Associated with Primary Monosymptomatic Nocturnal Enuresis" in the original guideline document.)

Chronic Headache

Inquiring about chronic headache in children with nocturnal enuresis is recommended **[B]**.

Epilepsy

An electroencephalogram is not justified in the assessment of nocturnal enuresis **[B]**.

Attention Deficit-Hyperactive Disorder (ADHD)

Given the high prevalence of these two conditions (ADHD and PMNE) and their association, it is clinically important to know if there is concomitant ADHD in

enuretic children. Hence, ADHD symptoms in children that present enuresis should be investigated **[B]**.

Other Psychological Problems

Early treatment of enuresis is recommended in Primary Care to improve **[A]** or prevent low self-esteem **[D]**.

Sleep/Arousal Disorders

Although waking up plays an important role in the pathogenesis of enuresis, no clinical implications have been found. Sleep patterns need not be studied as part of the clinical history of a child with enuresis **[B]**.

Sleep Apnoea Syndrome

It is recommended that a history of sleep apnoea symptoms in children with PMNE be obtained, despite the fact that the level of evidence is low **[C]**. It should always be ruled out in cases of secondary enuresis **[A]**.

Asthma/Allergy

It is not recommended that the presence of asthma/allergy in children with primary PMNE be specifically investigated **[C]**.

Caffeine

Although it has never been studied, it is reasonable to recommend that caffeine-containing beverages should be avoided late in the evening given their diuretic effect **[D]**.

Encopresis/Constipation

The presence/absence of constipation or encopresis is worth investigating in all patients with enuresis; if present, treat the constipation first **[C]**, since constipation is easy to diagnose on clinical grounds (fewer than 3 bowel movements per week), and given the possibility that constipation can be the cause of enuresis.

Pinworm Infestation

At present, and in the Primary Care setting, Graham's technique is not justified in all children with primary PMNE **[C]**.

Urinary Tract Infection/Bacteriuria

In PMNE, adopting the same attitude toward urinary tract infection/bacteriuria as in the general population is recommended **[B]**.

Diabetes Mellitus

Routine testing to rule out diabetes mellitus in children with PMNE is not recommended **[C]**.

Diabetes Insipidus

Routine testing to rule out diabetes insipidus in children with PMNE is not recommended **[D]**.

Detrusor Overactivity

The usefulness of anticholinergics in PMNE should be evaluated in clinical trials **[C]**.

Diagnosis

It is recommended that medical professionals actively search for cases (of PMNE) in all children 5 years of age or greater in any visit for illness or routine check-up. **[D]**.

Bladder Diary

It is essential that the bladder diary be filled in for at least 3 days **[A]**. It can be done conveniently over two weekends.

Dipstick Urinalysis

Urinary Infection

In monosymptomatic nocturnal enuresis, it is recommended that the same attitude toward urinary tract infection as in the general population be adopted **[B]**.

Diabetes Mellitus and Diabetes Insipidus

Routine testing to rule out diabetes mellitus in children with PMNE is not recommended **[C]**.

It is not recommended that dipstick urinalysis be used as a screening device for diabetes insipidus in children with PMNE **[B]**.

Treatment

How Efficacious Are Behavioral Interventions?

Simple Behavioural Interventions

Bladder retention training by toileting schedule does not provide any benefit in PMNE; hence, it is not recommended in Primary Care **[B]**.

Despite the lack of quality PMNE data, motivational therapy using charts with stars, drawings... helps to objectify the baseline situation regarding the number of wet nights and can be recommended before and together with other treatments, since it lacks adverse effects **[D]**.

There are no data available that evaluate the efficacy of bladder training by mid-stream urine interruption, and its use is not recommended in light of the fact that it can predispose to dysfunctional voiding **[D]**.

Complex and Educational Behavioural Interventions

Given the scant efficacy of complex and educational interventions, their use is not recommended in Primary Care **[B]**.

How Efficacious Is the Behavioral Intervention with Alarm Therapy?

Alarm/No Intervention

Alarm intervention is a treatment option for PMNE if the family is motivated and collaborative **[B]**.

Alarm/Alarm Associated with Other Behavioral Interventions

Associating bladder retention training by toileting schedule techniques or dry bed training with alarm therapy is not recommended **[B]**.

The reinforcement technique should be recommended before completing alarm therapy in children with PMNE **[B]**.

Tolerability

A change in treatment is recommended if, once alarm treatment has begun, the child never wakes up **[C]**. Monitoring this response over a minimum period of one month is recommended **[D]**.

How Efficacious Is Drug Treatment?

Desmopressin

Intranasal desmopressin should be administered at bedtime. Because orally administered desmopressin has its onset of action 30 minutes post-administration, it is recommended that it be taken 30 minutes before the last void and going to bed **[D]**.

Desmopressin versus Placebo

Drug treatment with desmopressin is a therapeutic option in PMNE **[B]**.

Dosage

Because the optimal dose of desmopressin is yet unknown, whether orally or intranasally administered, it is recommended to customize treatment to the minimum effective dose (0.2 to 0.4 mg oral and 10 to 40 micrograms intranasal). There are two trends: 1) to begin treatment with the minimum dose and titrate up if the response is insufficient, or 2) start directly with the higher dose, which can subsequently be titrated down, although there are no data that provide guidance as to when to do this **[D]**.

Tolerability

To prevent water intoxication, it is recommended that fluid intake the evening that desmopressin is taken be limited to no more than 240 ml (1 glass of water), 1 hour before to 8 hours after **[D]**.

Without taking cost-effectiveness studies into account, the oral mode of delivery is recommended because it is safer **[A]** and easier to administer, which improves treatment compliance **[D]**.

Treatment Duration

If the objective is to cure the condition, discontinuation should be started one month after attaining initial success **[B]**. In case of prolonged treatments, withdrawing therapy periodically for 1-2 weeks in order to re-evaluate is recommended **[D]**.

Relapses after Treatment Completion

Precipitous interruption of treatment with desmopressin that is achieving good response is not recommended **[B]**.

Using a structured withdrawal plan (at full doses) when finishing treatment with desmopressin is recommended **[B]**.

Association with Other Treatments

Except for specific situations in which there is great interest in achieving a higher rate of dryness at the beginning of treatment, routinely associating desmopressin and alarm is not recommended **[A]**.

In the case of children who wet the bed more than once a night, the use of desmopressin might be recommended with the aim of decreasing the number of nocturnal micturitions to just one, to make alarm therapy more tolerable **[D]**.

There is not enough evidence to recommend the association of anticholinergics, although it might be an alternative after treatment failures **[D]**.

Strategy with Alarm Therapy following Desmopressin Failure

Associating alarm therapy to desmopressin is not recommended in children who have not responded to desmopressin **[A]**.

Advantages and Disadvantages of Different Treatments

(See Table III "Advantages and Disadvantages of the Different Treatment Options" in the original guideline document.)

When the treatment objective is dryness in the short term, desmopressin and not alarm therapy is recommended **[A]**. If the aim is to maintain dryness without relapses when concluding treatment, alarm therapy offers obvious advantages over desmopressin **[A]**.

Prognostic Factors of Treatment

(See Tables IV and V "Predictive factors for alarm therapy" and "Predictive factors for treatment with desmopressin" in the original guideline document.)

Sex

Gender is not a prognostic factor to be taken into account when initiating therapy with alarm or desmopressin **[A]**.

Age

Age is not considered a decision criterion in treatment selection **[A]**.

Inheritance in Enuresis

Family history of enuresis does not intervene in the choice of treatment **[B]**.

It is recommended that alarm treatment not be started if low motivation is detected in the family or child **[B]**. In this case, desmopressin is the treatment of choice **[B]**.

Number of Wet Nights

Alarm therapy is a good treatment option when there is a high frequency of wet nights **[B]**. Based on the data in the literature, it is not possible to establish a precise number that defines "high frequency of wet nights", although it has been observed that the greater the number of wet nights, the better the response.

Desmopressin is a good treatment option when there are few wet nights **[B]**, even in young children **[B]**.

Number of Incidents Per Night

Determining maximum daytime voided volume (MDVV) by filling in bladder diaries is recommended **[A]**. Do not administer desmopressin in children with a MDVV less than 75% of the amount calculated by Koff's formula **[B]** and refer the child to the urologist if this volume is less than 45% **[C]** because it is a poor predictor for response to both treatments (desmopressin and alarm).

Family or Child Attitudes

It is recommended not starting alarm treatment if low motivation is detected in the family or the child **[B]**. In this case, desmopressin is the treatment of choice **[B]**.

Neuropsychological/Psychiatric Problems

In children with enuresis and the suspicion or diagnosis of ADHD or a psychiatric condition, it is recommended starting treatment with desmopressin instead of alarm **[B]**.

Rey-Osterrieth Complex Figure Test

Given the complexity of the test (time consuming and difficult to interpret), the guideline developers do not consider it to be helpful in clinical practice, and therefore do not recommend its use in Primary Care **[D]**.

Hypercalciuria

There is not sufficient evidence to recommend urinary calcium (Ca)/creatinine ratio determinations in children with PMNE and nocturnal polyuria in Primary Care, although it could be examined in those children who have failed on desmopressin **[D]**.

Definitions:

Grades of Recommendation*

A. Consistent level 1 studies
B. Consistent level 2 or 3 studies or extrapolations from level 1 studies
C. Level 4 studies or extrapolations from level 2 or 3 studies
D. Level 5 evidence or troublingly inconsistent or inconclusive studies of any level

* See the "Rating Scheme for the Strength of the Evidence" field for the definitions of the levels of evidence.

CLINICAL ALGORITHM(S)

A "Diagnostic Algorithm" and a "Treatment Algorithm" are provided in the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment of nocturnal enuresis may eliminate many of the negative repercussions for the child and his/her family, including problems with the child's social relations, social performance, and self-esteem.

POTENTIAL HARMS

Side effects of desmopressin are very uncommon and almost never require treatment withdrawal. The adverse effect that can and must be prevented is water intoxication. Since 1974, twenty-eight cases have been reported, all with intranasal administration.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The authors of the present guide assume that the healthcare professionals will exercise their clinical discretion and general knowledge in applying the general and specific recommendations to each individual patient. The recommendations may not be appropriate in all circumstances. All the recommendations contained in these guidelines shall only be applied in the absence of contraindications, adverse effects, or treatment interactions.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Clinical Algorithm
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Asociación Española de Pediatría de Atención Primaria (AEPap). Evidence-based clinical practice guidelines: primary monosymptomatic nocturnal enuresis in primary care. Rev Pediatr Atencion Prim 2005 Oct;VII(Suppl 3):1-149.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Oct

GUIDELINE DEVELOPER(S)

Spanish Association of Primary Care Pediatrics

SOURCE(S) OF FUNDING

Spanish Association of Primary Care Pediatrics

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All authors work for the Agencia Valenciana de Salud (Valencian Regional Government Health Authority) of the Generalitat Valenciana (Valencian Regional

Government). They have no relationship whatsoever with private commercial entities involved in the treatment of enuresis nor have they received any external public or private assistance in relation to these guidelines. These guidelines have been promoted and carried out by the authors without any external financial support.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: None available

Print copies: Available from Exlibris Ediciones. C/ Infanta Mercedes, 92, bajo; 28020 Madrid; Tel.: 915717051; Fax: 915716913; Email: revistapap@pap.edu

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Asociación Española de Pediatría de Atención Primaria (AEPap). Quick reference guide. Evidence-based clinical practice guidelines: primary monosymptomatic nocturnal enuresis in primary care. Rev Pediatr Atencion Prim 2005 Oct;VII(Suppl 3):31-44

Annexes 2 and 3 of the original guideline document contain diagnostic criteria for attention deficit hyperactivity disorder (ADHD) and a diagnostic questionnaire for dysfunctional voiding.

PATIENT RESOURCES

None available

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